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(57) Abstract

One aspect of the present invention is a method of human female menopause treatment which comprises subcutaneous administration of a menopausely effective amount of a hormonal replacement agent selected from the group consisting of a progestogen and a progestogen plus an estrogen. Another aspect of the present invention is treating endometriosis.

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SUBCUTANEOUS MEDROXYPROGESTERONE ACETATE FOR TREATMENT OF MENOPAUSE AND ENDOMETRIOSIS

BACKGROUND OF THE INVENTION

1. Field of the Invention

The present invention is a subcutaneous method for administering a progestogen or a progestogen and an estrogen for female contraceptive use or for female menopause treatment. The present invention is also a method for subcutaneous administration of a progestogen for the treatment of endometriosis.

2. Description of the Related Art

US Patent 3,377,364 (Example 9) discloses medroxyprogesterone acetate.

The 1996 Physicians Desk Reference (PDR), pages 2602-2604, discloses that DEPO-PROVERA, a sterile aqueous suspension of medroxyprogesterone acetate for IM administration, produces a contraceptive effect for three months in females. Following the three month contraceptive period, the female has a menstrual period and is again fertile unless she has another IM injection prior to her period.

The *J. Reprod. Fertil.*, 15, 209-14 (1968) discloses a clinical study of medroxyprogesterone acetate (25 mg) and estradiol cypionate (5 mg) by monthly IM injection for female contraception in 104 women over a period of from four to 15 mo with no pregnancies. Following each IM injection there is a contraceptive effect for a one month time period following which the female has a menstrual period. *Contraception*, 56, 353-359 (1997) also discloses a clinical study of medroxyprogesterone acetate (25 mg) and estradiol cypionate (5 mg) by monthly IM injection for female contraception.

These two methods work well to provide contraception to ovulating females who wish to have sexual intercourse and not get pregnant. The major problem is that in both cases the injection is IM and IM injections should be administered not by the patient but by an appropriately trained health care professional. The method of the present invention does not rely on IM administration but rather subcutaneous administration which can be done by the patient.

In treating menopause or the symptoms of menopause the standard therapy is estrogen or estrogen plus progestogen administered orally on a daily basis. US Patent 4,826,831 discloses a method of hormonal treatment of menopausal women using either a progestogen, including medroxyprogesterone acetate, and estrogen by oral or intramuscular injection as well as by an implantable composition.

Endometriosis is the presence and growth of endometrial tissue outside the internal uterine lining. It is know to those skilled in the art that progestogens can be administered orally to treat this condition. The present invention does not use oral administration.

SUMMARY OF INVENTION

Disclosed is a method of human female menopause treatment which comprises subcutaneous administration of a menopausely effective amount of a hormonal replacement agent selected from the group consisting of a progestogen and a progestogen plus an estrogen.

Also disclosed is a method of treating endometriosis in a human female who is in need of such treatment which comprises subcutaneous administration of a endometrially effective amount of a progestogen.

DETAILED DESCRIPTION OF THE INVENTION

The present invention is a method of human female contraception which comprises subcutaneous administration of a contraceptively effective amount of a contraceptive agent selected from the group consisting of a progestogen and a progestogen plus an estrogen.

The method of the present invention can be practiced by the female patient herself administering the subcutaneous injection herself. To provide contraception, the patient should be taught by a trained health care professional how to administer the subcutaneous injection of progestogen or progestogen plus estrogen. The patient then injects subcutaneously a contraceptively effective amount as she was directed either approximately once a month or approximately every three months or approximately every six months. The word "approximately" is used because some months have 30 days while others have 31 days. In addition, it is not critical if the female is off by one to three days from the exact time to administer the subcutaneous injection because of any reason.

There are two ways to practice the claimed invention. These are either the administration of a progestogen alone or the combination of a progestogen with an estrogen. When administering the progestogen alone it is administered either once a month, or up to approximately every six months or any interval in between, depending on the dose. When the patient uses the three or six months methods, she will not have a menstrual period during that time. When progestogen alone method is utilized it is preferred that the female administer the subcutaneous injection either approximately every three or approximately every six months. At the end of the one month, three month or six month time period normal fertility returns unless the patient uses another injection or some other form of fertility control.

Alternatively, the method of the present invention can be practiced by the administration of a combination of a progestogen plus an estrogen once a month. When this method is utilized the female will have a menstrual period every month. At the end of each month time period, normal fertility returns unless the patient uses another injection or some other form of fertility control.

The pharmaceutical formulations necessary to practice the present invention are known. US Patent 4,038,389 discloses a 200-600 mg/ml parenteral formulation of medroxyprogesterone acetate. The 1996 Physicians Desk Reference (PDR), pages 2602-2604, discloses a sterile aqueous suspension of medroxyprogesterone acetate (DEPO-PROVERA) for depot IM administration for female contraception containing 150 mg of medroxyprogesterone acetate/ml. The parenteral formulation can be administered once every month or every 13 weeks (3 months) or every 26 weeks (6 months). Following the contraceptive period, the female has a menstrual period unless she has another IM injection prior to her period. The female may have a series of IM injections of medroxyprogesterone acetate to provide contraception on a continuous basis. The *J. Reprod. Fertil.*, 15, 209-14 (1968) discloses a formulation of medroxyprogesterone acetate (25 mg) and estradiol cypionate (5 mg) which was used in a clinical study by monthly IM injection for female contraception. See also *Contraception*, 49, 293-301 (1994) at 296 and *Contraception*, 56, 353-359 (1997) at 353.

It is preferred that the progestogen be selected from the group consisting of medroxyprogesterone acetate, progesterone, norethindrone, desogestrel and levo-norgestrel it is more preferred that the progestogen be medroxyprogesterone acetate. It is preferred that the estrogen be selected from the group consisting of ethinyl estradiol, estradiol cypionate and estradiol valerate; it is more preferred that the estrogen be estradiol cypionate.

It is preferred that the contraceptive agent be medroxyprogesterone acetate or medroxyprogesterone acetate plus estradiol cypionate.

When the contraceptive method of the present invention is practiced by using a progestogen alone, it is preferred that the progestogen be in a depot form as is well known to those skilled in the art. It is preferred that the contraceptively effective amount for one month be for medroxyprogesterone acetate from about 10 mg to about 50 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female; for three months be for

medroxyprogesterone acetate from about 50 mg to about 200 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female and for six months be for medroxyprogesterone acetate from about 100 mg to about 500 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female. When the progestogen is medroxyprogesterone acetate it is preferred that the dose for one, three and six monthes be from about 20 mg to about 30 mg/female, from about 75 mg to about 175 mg/female and from about 150 mg to about 300 mg/female. Alternatively, and operable but less preferred, at three months the medroxyprogesterone acetate dose is from about 100 mg to about 200 mg/female; at six months the medroxyprogesterone acetate dose is from about 200 mg to about 500 mg/female. Within this alternative range, it is preferred that the medroxyprogesterone acetate dose for three months be from about 125 mg to about 175 mg/female and for six months from about 250 mg to about 300 mg/female.

When the contraceptive method of the present invention is practice by using a progestogen plus an estrogen once a month, the progestogen and estrogen should be in a formulation suitable for subcutaneous administration as is known to those skilled in the art. It is preferred that the contraceptively effective amount be:

for medroxyprogesterone acetate from about 10 mg to about 50 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

and the contraceptively effective amount of estrogen is:

for estradiol cypionate from about 2.5 mg to about 20 mg/female,
ethinyl estradiol from about 0.5 mg to about 3 mg/female,
estradiol valerate from about 2.5 mg to about 20 mg/female. It is preferred the contraceptively effective amount of medroxyprogesterone acetate is from about 20 mg to about 30 mg/female and the contraceptively effective amount of estradiol cypionate is from about 3 to about 10 mg/female.

The present invention is a method of human female menopause treatment which comprises subcutaneous administration of a menopausely effective amount of a hormonal

replacement agent selected from the group consisting of a progestogen and a progestogen plus an estrogen.

The method of the present invention can be practiced by the female patient herself administering the subcutaneous injection herself. To provide menopause treatment, the patient should be taught by a trained health care professional how to administer the subcutaneous injection of progestogen or progestogen plus estrogen. The patient then injects subcutaneously a menopausely effective amount as she was directed either approximately once a month or approximately every three months or approximately every six months. The word "approximately" is used because some months have 30 days while others have 31 days. In addition, it is not critical if the female is off by one to three days from the exact time to administer the subcutaneous injection because of any reason.

There are two ways to practice the claimed invention. These are either the administration of a progestogen alone or the combination of a progestogen with an estrogen. When administering the progestogen alone it is administered either once a month, or approximately every three months or approximately every six months. When the patient uses the three or six months methods, she will not have a menstrual period during that time. When progestogen alone method is utilized it is preferred that the female administer the subcutaneous injection either approximately every three or approximately every six months.

Alternatively, the method of the present invention can be practiced by the administration of a combination of a progestogen plus an estrogen once a month. When this method is utilized the female will have a menstrual period every month.

The pharmaceutical formulations necessary to practice the present invention are discussed above and are well known to those skilled in the art.

It is preferred that the progestogen be selected from the group consisting of medroxyprogesterone acetate, progesterone, norethindrone, desogestrel and levo-norgestrel it is more preferred that the progestogen be medroxyprogesterone acetate. It is preferred that the estrogen be selected from the group consisting of ethinyl estradiol, estradiol cypionate and estradiol valerate; it is more preferred that the estrogen be estradiol cypionate.

It is preferred that the hormonal replacement agent be medroxyprogesterone acetate or medroxyprogesterone acetate plus estradiol cypionate.

When the menopausal treatment of the present invention is practiced by using a progestogen alone, it is preferred that the progestogen be in a depot form as is well known to those skilled in the art. It is preferred that the menopausely effective amount for one

month be for medroxyprogesterone acetate from about 10 mg to about 50 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female; for three months be for medroxyprogesterone acetate from about 50 mg to about 200 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female and for six months be for medroxyprogesterone acetate from about 100 mg to about 500 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female. When the progestogen is medroxyprogesterone acetate it is preferred that the dose for one, three and six monthes be from about 20 mg to about 30 mg/female, from about 75 mg to about 175 mg/female and from about 150 mg to about 300 mg/female. Alternatively, and operable but less preferred, at three months the medroxyprogesterone acetate dose is from about 100 mg to about 200 mg/female; at six months the medroxyprogesterone acetate dose is from about 200 mg to about 500 mg/female. Within this alternative range, it is preferred that the medroxyprogesterone acetate dose for three months be from about 125 mg to about 175 mg/female and for six months from about 250 mg to about 300 mg/female.

When the menopause treatment of the present invention is practice by using a progestogen plus an estrogen once a month, the progestogen and estrogen should be in a formulation suitable for subcutaneous administration as is known to those skilled in the art. It is preferred that the menopausely effective amount be:

for medroxyprogesterone acetate from about 10 mg to about 50 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

and the menopausely effective amount of estrogen is:

for estradiol cypionate from about 2.5 mg to about 20 mg/female,
ethinyl estradiol from about 0.5 mg to about 3 mg/female,
estradiol valerate from about 2.5 mg to about 20 mg/female. It is preferred the menopsausely effective amount of medroxyprogesterone acetate is from about 20 mg to

about 30 mg/female and the menopausely effective amount of estradiol cypionate is from about 3 to about 10 mg/female.

Another aspect of the present invention is a method of treating endometriosis in a human female who is in need of such treatment which comprises subcutaneous administration of a endometrially effective amount of a progestogen.

The method of the present invention can be practiced by the female patient herself administering the subcutaneous injection herself. To provide effective treatment, the patient should be taught by a trained health care professional how to administer the subcutaneous injection of progestogen. The patient then injects subcutaneously an endometrially effective amount as she was directed either approximately once a month or approximately every three months or approximately every six months. The word "approximately" is used because some months have 30 days while others have 31 days. In addition, it is not critical if the female is off by one to three days from the exact time to administer the subcutaneous injection because of any reason.

When administering the progestogen, it is administered either once a month, or approximately every three months or approximately every six months. When the patient uses the three or six months methods, she will not have a menstrual period during that time. It is preferred that the female administer the subcutaneous injection either approximately every three or approximately every six months.

The pharmaceutical formulations necessary to practice the present invention are discussed above and are well known to those skilled in the art.

It is preferred that the progestogen be selected from the group consisting of medroxyprogesterone acetate, progesterone, norethindrone, desogestrel and levo-norgestrel it is more preferred that the progestogen be medroxyprogesterone acetate.

When the endometriosis treatment of the present invention is practiced, it is preferred that the progestogen be in a depot form as is well known to those skilled in the art. It is preferred that the endometrially effective amount for one month be for medroxyprogesterone acetate from about 10 mg to about 50 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female; for three months be for medroxyprogesterone acetate from about 50 mg to about 200 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2

mg/female and for six months be for medroxyprogesterone acetate from about 100 mg to about 500 mg/female, for progesterone from about 25 mg to about 200 mg/female, for northindrone from about 5 mg to about 50 mg/female, for desogestrel from about 1 mg to about 4 mg/female, for levo-norgrestrel from about 0.5 mg to about 2 mg/female. When the progestogen is medroxyprogesterone acetate it is preferred that the dose for one, three and six months be from about 20 mg to about 30 mg/female, from about 75 mg to about 175 mg/female and from about 150 mg to about 300 mg/female. Alternatively, and operable but less preferred, at three months the medroxyprogesterone acetate dose is from about 100 mg to about 200 mg/female; at six months the medroxyprogesterone acetate dose is from about 200 mg to about 500 mg/female. Within this alternative range, it is preferred that the medroxyprogesterone acetate dose for three months be from about 125 mg to about 175 mg/female and for six months from about 250 mg to about 300 mg/female.

The exact dosage and frequency of administration of the progestogen or progestogen plus estrogen for contraception, menopause or endometriosis treatment depends on the age, weight, general physical condition of the particular patient, other medication the individual may be taking as is well known to those skilled in the art and can be more accurately determined by measuring the blood level or concentration of the progestogen or progestogen and estrogen in the patient's blood and/or the patient's response to the particular condition being treated.

DEFINITIONS

The definitions and explanations below are for the terms as used throughout this entire document including both the specification and the claims.

Medroxyprogesterone acetate refers to 17α-hydroxy-6α-methylpregn-4-ene-3,20-dione 17-acetate.

IM refers to intramuscular injection.

Menopause refers to, and includes, premenopause, menopause and postmenopause.

EXAMPLES

Without further elaboration, it is believed that one skilled in the art can, using the preceding description, practice the present invention to its fullest extent. The following detailed examples describe how to prepare the various compounds and/or perform the various processes of the invention and are to be construed as merely illustrative, and not limitations of the preceding disclosure in any way whatsoever. Those skilled in the art will promptly recognize appropriate variations from the procedures both as to reactants and as to reaction conditions and techniques.

EXAMPLE 1 23 Year Old Female - One Month Progestogen

A 60 kg 23 year old female who desires to have sexual intercourse on a regular basis is shown how to give a subcutaneous injection by her physician. She injects 0.2 ml of a 100 mg/ml of an aqueous suspension of medroxyprogesterone acetate subcutaneous as instructed on the third day of her menstrual period. She has sexual intercourse twice a week with a fertile male and does not become pregnant.

EXAMPLE 2 37 Year Old Female - Three Month Progestogen

A 78 kg 37 year old female who desires to have sexual intercourse on a regular basis is shown how to give a subcutaneous injection by her physician's nurse. She injects 1.0 ml of a 125 mg/ml of an aqueous suspension of medroxyprogesterone acetate subcutaneous as instructed on the second day of her menstrual period. She has sexual intercourse three times a week with a fertile male and does not become pregnant.

EXAMPLE 3 21 Year Old Female - Six Month Progestogen

A 67 kg 21 year old female who desires to have sexual intercourse on a regular basis is shown how to give a subcutaneous injection by her gynecologist. She injects 1.0 ml of a 250 mg/ml of an aqueous suspension of medroxyprogesterone acetate subcutaneous as instructed on the third day of her menstrual period. She has sexual intercourse for six months with an average of three and a half times a week with a fertile male and does not become pregnant.

EXAMPLE 4 40 Year Old Female - Progestogen Plus Estrogen

A 71 kg 40 year old female who desires to have sexual intercourse on a regular basis is shown how to give a subcutaneous injection by her physician's nurse. She injects 0.5 ml of an aqueous suspension containing 20 mg medroxyprogesterone acetate and 7.0 mg estradiol cypionate as instructed on the second day of her menstrual period. She has sexual intercourse three times a week with a fertile male and does not become pregnant.

CLAIMS

1. A method of human female menopause treatment which comprises subcutaneous administration of a menopausely effective amount of a hormonal replacement agent selected from the group consisting of a progestogen and a progestogen plus an estrogen.

2. A method of human female menopause treatment according to claim 1 where the progestogen is selected from the group consisting of medroxyprogesterone acetate, progesterone, norethindrone, desogestrel and levo-norgestrel.

3. A method of human female menopause treatment according to claim 2 where the progestogen is medroxyprogesterone acetate.

4. A method of human female menopause treatment according to claim 1 where the estrogen is selected from the group consisting of ethinyl estradiol, estradiol cypionate and estradiol valerate.

5. A method of human female menopause treatment according to claim 4 where the estrogen is estradiol cypionate.

6. A method of human female menopause treatment according to claim 1 where the hormonal replacement agent is medroxyprogesterone acetate.

7. A method of human female menopause treatment according to claim 1 where the hormonal replacement is medroxyprogesterone acetate plus estradiol cypionate.

8. A method of human female menopause treatment according to claim 1 where when the menopausely effective amount of progestogen is administered once a month the menopausely effective amount is:

for medroxyprogesterone acetate from about 10 mg to about 50 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

9. A method of human female menopause treatment according to claim 8 where the menopausely effective amount of medroxyprogesterone acetate is from about 20 mg to about 30 mg/female.

10. A method of human female menopause treatment according to claim 1 where when the menopausely effective amount of progestogen is administered every three months the menopausely effective amount is:

for medroxyprogesterone acetate from about 50 mg to about 200 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

11. A method of human female menopause treatment according to claim 10 where the menopausely effective amount of medroxyprogesterone acetate is from about 75 mg to about 175 mg/female.

12. A method of human female menopause treatment according to claim 1 where when the menopausely effective amount of progestogen is administered every three months the menopausely effective amount is:

for medroxyprogesterone acetate from about 100 mg to about 200 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

13. A method of human female menopause treatment according to claim 12 where the menopausely effective amount of medroxyprogesterone acetate is from about 125 mg to about 175 mg/female.

14. A method of human female menopause treatment according to claim 1 where when the menopausely effective amount of progestogen is administered every six months the menopausely effective amount is:

for medroxyprogesterone acetate from about 100 mg to about 500 mg/female,

for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

15. A method of human female menopause treatment according to claim 14 where the menopausely effective amount of medroxyprogesterone acetate is from about 150 mg to about 300 mg/female.

16. A method of human female menopause treatment according to claim 1 where when the menopausely effective amount of progestogen is administered every six months the menopausely effective amount is:

for medroxyprogesterone acetate from about 200 mg to about 500 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

17. A method of human female menopause treatment according to claim 16 where the menopausely effective amount of medroxyprogesterone acetate is from about 250 mg to about 300 mg/female.

18. A method of human female menopause treatment according to claim 1 where both the progestogen and estrogen are administered once every month the menopausely effective amount of progestogen is

for medroxyprogesterone acetate from about 10 mg to about 50 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

and the menopausely effective amount of estrogen is

for estradiol cypionate from about 2.5 mg to about 20 mg/female,
ethinyl estradiol from about 0.5 mg to about 3 mg/female,
estradiol valerate from about 2.5 mg to about 20 mg/female.

19. A method of human female menopause treatment according to claim 18 where the menopausely effective amount of medroxyprogesterone acetate is from about 20 mg to about 30 mg/female and the menopausely effective amount of estradiol cypionate is from about 3 to about 10 mg/female.

20. A method of human female menopause treatment according to claim 1 where the menopausely effective amount of progestogen is administered either approximately every 3 or approximately every 6 months.

21. A method of human female menopause treatment according to claim 1 where the menopause treatment is for premenopause.

22. A method of human female menopause treatment according to claim 1 where the menopause treatment is for menopause.

23. A method of human female menopause treatment according to claim 1 where the menopause treatment is for postmenopause.

24. A method of human female menopause treatment according to claim 1 where the subcutaneous administration of the menopausely effective amount of a hormonal replacement agent is by self administration.

25. A method of treating endometriosis in a human female who is in need of such treatment which comprises subcutaneous administration of a endometrially effective amount of a progestogen.

26. A method of treating endometriosis in a human female according to claim 25 where the progestogen is selected from the group consisting of medroxyprogesterone acetate, progesterone, norethindrone, desogestrel and levo-norgestrel.

27. A method of treating endometriosis in a human female according to claim 26 where the progestogen is medroxyprogesterone acetate.

28. A method of treating endometriosis in a human female according to claim 25 where when the endometrially effective amount of progestogen is administered once a month and is:

for medroxyprogesterone acetate from about 10 mg to about 50 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

29. A method of treating endometriosis in a human female according to claim 28 where the endometrially effective amount of medroxyprogesterone acetate is from about 20 mg to about 30 mg/female.

30. A method of treating endometriosis in a human female according to claim 25 where when the endometrially effective amount of progestogen is administered every three months and is:

for medroxyprogesterone acetate from about 50 mg to about 200 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

31. A method of treating endometriosis in a human female according to claim 30 where the endometrially effective amount of medroxyprogesterone acetate is from about 75 mg to about 175 mg/female.

32. A method of treating endometriosis in a human female according to claim 25 where when the endometrially effective amount of progestogen is administered every three months and is:

for medroxyprogesterone acetate from about 100 mg to about 200 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

33. A method of treating endometriosis in a human female according to claim 32 where the endometrially effective amount of medroxyprogesterone acetate is from about 125 mg to about 175 mg/female.

34. A method of treating endometriosis in a human female according to claim 25 where when the endometrially effective amount of progestogen is administered every six months an is:

for medroxyprogesterone acetate from about 100 mg to about 500 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

35. A method of treating endometriosis in a human female according to claim 34 where the endometrially effective amount of medroxyprogesterone acetate is from about 150 mg to about 300 mg/female.

36. A method of treating endometriosis in a human female according to claim 25 where when the endometrially effective amount of progestogen is administered every six months an is:

for medroxyprogesterone acetate from about 200 mg to about 500 mg/female,
for progesterone from about 25 mg to about 200 mg/female,
for northindrone from about 5 mg to about 50 mg/female,
for desogestrel from about 1 mg to about 4 mg/female,
for levo-norgrestrel from about 0.5 mg to about 2 mg/female.

37. A method of treating endometriosis in a human female according to claim 36 where the endometrially effective amount of medroxyprogesterone acetate is from about 250 mg to about 300 mg/female.

38. A method of treating endometriosis in a human female according to claim 25 where the endometrially effective amount of progestogen is administered either approximately every 3 or approximately every 6 months.

39. A method of treating endometriosis in a human female according to claim 25 where the endometrially effective amount of progestogen is administered by self administration.